

REMARKS

Claims 4, 5, 7, 8, and 11 have been amended to correct clerical errors. Previous claims 15-19 were not entered. New claims 20-24 have been added. Support for the new claims can be found, for example, at page 8, lines 15-24, and at pages 15-17 of the specification. No new matter has been added. The amendments raise no new issues that will require further consideration and/or search and only narrow the scope of the claims and do not touch the merits of the application within the meaning of 37 C.F.R. 1.116(b). Claims 1-11 and 15-19 are pending. Claims 1, 8 and 16 are independent.

Applicants thank the Examiner for withdrawing the previous rejections under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 102(b)

Claims 1-11 have been rejected under 35 U.S.C. § 102(b) as being unpatentable over Japan Patent No. 7-318,551 ("JP '551"). See page 2 of the Office Action. The Examiner states that "[t]he claims are considered to read on Japan Patent No. 7-318,551."

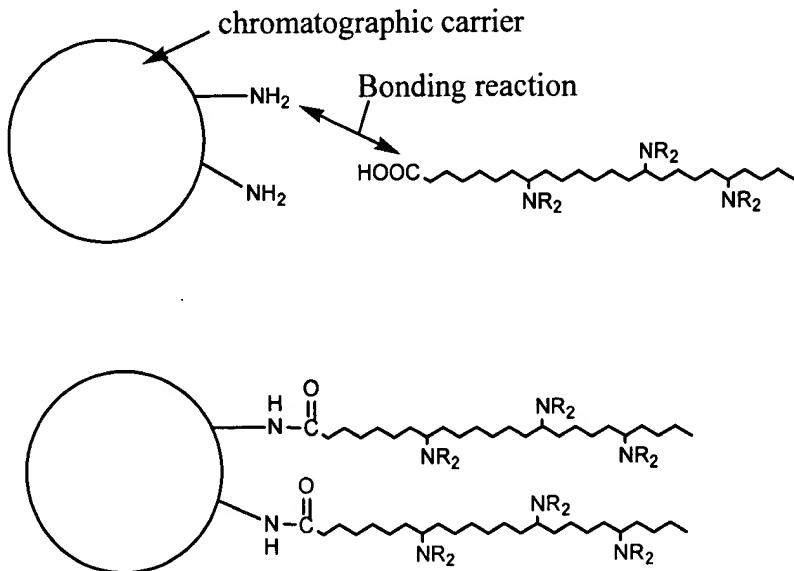
Applicants respectfully disagree. As discussed below, the structure of the chromatographic packing and the method of separating substances are not anticipated by JP '551.

Independent claim 1 and claims that depend therefrom

Applicants have discovered a method of separating substances. The method includes **chromatographically separating the substances with the use of a packing which contains a charged (co)polymer and makes it possible to change the effective charge density on the surface of a stationary phase by a physical stimulus.** See independent claim 1.

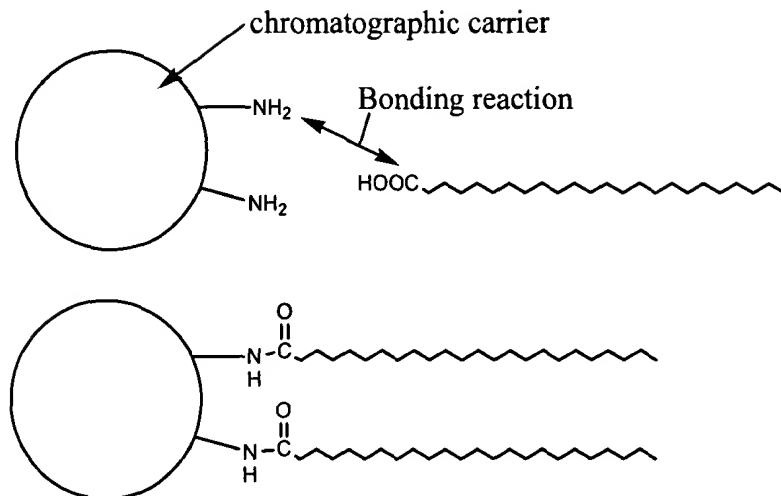
The charged (co)polymer can have ionizable groups in the side chains and/or at the ends that can become charged. The charged groups on the side chains have an effect on chromatographically separating substances. A terminal group, i.e. one at the end of the polymer, is consumed in a bonding reaction to a chromatographic carrier. See Scheme I below. Because the polymer has ionizable groups in the side chains as well at the ends, the polymer retains

additional, unreacted ionizable groups after the bonding reaction is complete, as depicted in Scheme I. Positive or negative ionizable groups can be included in the polymer. The specification at page 8, lines 15-24, lists examples of monomers that can provide ionizable groups in the side chains of the charged (co)polymer.



**Scheme I**

The Examiner contends that JP '551 discloses "that the poly(N-isopropylacrylamide) has been modified with amino, carboxyl, or hydroxyl groups." See Office Action at page 3. JP '551 describes a chromatographic carrier where "the carrier surface is chemically modified with a temperature responsive polymer, for example, a polyalkylacrylamide having a terminal amino, carboxyl, or hydroxyl group" (JP '551, at page 8, emphasis added). The terminal amino, carboxyl, or hydroxyl group is consumed in the bonding reaction to the chromatographic carrier. As taught in JP '551, once the bonding reaction is complete, the temperature-responsive polymer has no ionizable groups nor any charged groups, as depicted in Scheme II.



**Scheme II**

Thus, JP '551 does not describe a charged (co)polymer. The chromatographic material of JP '551 does not possess a charged (co)polymer. JP '551 does not describe a method for separating substances using a packing that contains a charged (co)polymer that changes the effective charge density on the surface of the stationary phase by a physical stimulus. Thus, JP '551 does not anticipate independent claim 1 and claims that depend therefrom. Applicants respectfully request reconsideration and withdrawal of this rejection.

Independent claim 8 and claims that depend therefrom

Applicants have discovered a method for separating substances. The method includes retaining substances using a stationary phase including a chromatographic packing chemically modified with a polyalkylacrylamide copolymer having an amino group, a carboxyl group, or a hydroxyl group and changing the hydrophilic/hydrophobic balance on the surface of the stationary phase by a temperature gradient method wherein the external temperature is changed stepwise. See independent claim 8.

JP '551 does not describe a stationary phase made of a chromatographic material chemically modified with a polyalkylacrylamide copolymer having an amino group, a carboxyl group, or a hydroxyl group and changing the hydrophilic/hydrophobic balance on the surface of

the stationary phase by the temperature gradient method wherein the external temperature is changed stepwise. While JP '551 describes packing material having a reactive group, the reactive group is needed to bond a temperature-responsive polymer to the surface of the chromatographic packing. See Scheme II above and paragraph 6 of JP '551. There is no description of changing the hydrophilic/hydrophobic balance on the surface of the stationary phase by the temperature gradient method wherein the external temperature is changed stepwise. There is also no description of a stationary phase being made of a packing chemically modified with a polyalkylacrylamide copolymer having an amino group, a carboxyl group, or a hydroxyl group. See Formula 3 of JP '551. Thus, JP '551 does not anticipate independent claim 8 and claims that depend therefrom. Applicants respectfully request reconsideration and withdrawal of this rejection.

**Rejection under 35 U.S.C. § 103(a)**

The Examiner has rejected claims 1-11 under 35 U.S.C. § 103(a) as unpatentable over JP '551. See page 2 of the Office Action. The Examiner asserts that "...if a difference exists between the claims and Japan Patent No. 7-318,551, it would reside in optimizing the steps of Japan Patent No. 7-318,551. It would have been obvious to optimize the steps of Japan Patent No. 7-318,551 to enhance separation." Applicants respectfully disagree.

**Independent claim 1 and claims that depend therefrom**

Applicants' method for separating substances described in claim 1 changes the effective charge density on the surface of the stationary phase, making it possible to perform two chromatographic modes, for example, ion-exchange chromatography and reversed phase chromatography, with the stationary phase. See page 6, lines 1-9 of the specification. Substances which have not been able to be separated by conventional methods can be separated by the method. See, for example, page 4, lines 16-23 and page 6, lines 17 through page 7, line 6 of the specification.

JP '551 does not teach or suggest a charged polymer or copolymer that changes the effective charge density on the surface of the stationary phase by a physical stimulus. The materials described in JP '551 are packing materials having modified surfaces. The modified surfaces include reactive groups to which are bonded a temperature-responsive polymer. See Formula 3 of JP '551. However, there is no teaching or suggestion in JP '551 to include a charged (co)polymer in a stationary phase that changes the effective charge density on the surface of the stationary phase. Nothing in JP '551 provides motivation to a person of ordinary skill to include a charged (co)polymer on the packing for any reason. Based on the teachings of JP '551, a person of ordinary skill in the art would not use a charged (co)polymers in a packing. Thus, independent claim 1 and claims that depend therefrom are patentable over JP '551. Applicants respectfully request reconsideration and withdrawal of this rejection.

Independent claim 8 and claims that depend therefrom

For similar reasons, JP '551 does not teach or suggest the method of claim 8. JP '551 does not teach or suggest a stationary phase made of a chromatographic material chemically modified with a polyalkylacrylamide copolymer having an amino group, a carboxyl group, or a hydroxyl group or changing the hydrophilic/hydrophobic balance on the surface of the stationary phase by the temperature gradient method wherein the external temperature is changed stepwise. JP '551 teaches a polyalkylacrylamide that does not have an amino, carboxyl or hydroxyl group. See Formula 1 of JP '551. There is no teaching or suggestion in JP '551 to include a polyalkylacrylamide copolymer having an amino group, a carboxyl group, or a hydroxyl group in a stationary phase. Nothing in JP '551 would motivate a person of ordinary skill to chemically modify packing with a polyalkylacrylamide copolymer having an amino group, a carboxyl group, or a hydroxyl group on the surface of chromatographic packing for any reason. Based on the teachings of JP '551, a person of ordinary skill in the art would not be motivated to use a polyalkylacrylamide copolymer having an amino group, a carboxyl group, or a hydroxyl group to chemically modify chromatographic packing. Thus, independent claim 8 and claims that

depend therefrom are patentable over JP '551. Applicants respectfully request reconsideration and withdrawal of this rejection.

**New independent claim 16 and claims that depend therefrom**

Claim 16 is directed to a method of separating substances with that includes the use of a packing chemically modified with a polyalkylacrylamide polymer or copolymer having a **plurality of amino groups, a plurality of carboxyl groups, or a plurality of hydroxyl groups** in the side chains or at the ends. None of the cited references disclose, teach, or suggest a packing chemically modified with a polyalkylacrylamide polymer or copolymer having a plurality of amino groups, a plurality of carboxyl groups, or a plurality of hydroxyl groups in the side chains or at the ends. Independent claim 16 and claims that depend therefrom are patentable over the cited references.

**CONCLUSION**

Applicants respectfully request that all claims be allowed. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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